1. Newly added claims 105,111,112,116-118,125 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species that do not have the amino acid sequence encompassed by the previously elected species, there being no allowable generic or linking claim. Election was previously made **without** traverse in the reply filed on 11/10/08.

2. Claims 103,104,106-110,113-115,119-124,126-134 are under consideration.

3. The previously pending rejections are withdrawn in view of the cancellation of the previously pending claims.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 103,104,106-109,113,119,120,123,124,126,127,129-134 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of claimed invention.

The claimed antibody encompasses antibodies with a single defined CDR (aka CDR3) and/or undefined FR regions. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity, which is characteristic of the immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA, 79(6):1979-1983, March 1982). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. MacCallum, et al. (Journal of Molecular Biology, 1996. Vol. 262, pages 732-745) analyzed many different antibodies for interactions with antigen and state that although CDR3 of the heavy and light chain dominate, a number of residues outside the standard CDR definitions make antigen contacts (see page 733, right column) and non- contacting residues within the CDRs coincide with residues as important in defining canonical backbone conformations (see page 735, left column). De Pascalis, et al. (Journal of Immunology, 2002. Vol. 169, pages 3076-3084) demonstrate that grafting of the CDRs into a human framework was performed by grafting CDR residues and maintaining framework residues that were deemed essential for preserving the structural integrity of the antigen binding site (see page 3079, right column). Although abbreviated CDR residues were used in the constructs, some residues in all 6 CDRs were used for the constructs (see page 3080, left column). Thus it is unpredictable as to what amino acids can be substituted into the original intact antibodies disclosed in the specification wherein the antibodies would still have the functional properties recited in the claims. Thus, the written description provided in the specification is not commensurate with the scope of the claimed inventions. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University

of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

Regarding applicants comments, none of the cited references are germane to the instant rejection wherein an antibody binds CD20 (a protein antigen) recites a single CDR3 amino acid sequence and wherein the amino acid sequences of the other CDRs are unknown and unpredictable. Regarding applicants comments about Barbas et al. (1995), said reference does not address the issue under consideration because it

relates to antibodies which bind DNA, not a protein such as CD20. Said antibodies differ from antiprotein antibodies in that said antibodies are crossreactive and bind a variety of antigens (aka see Figure 2). Furthermore, the tetanus toxoid antibody which received the CDR3 regions had already been selected as permissive for DNA binding (aka, said unmodified antibody could crossreact with DNA)(see page 2532, second column). In addition, it was unpredictable as to whether a particular CDR3 region would mediate binding even in the particular system reported by Barbas et al. (1995) (see page 2532, second column regarding antibody SI-32). Ditzel et al. refers to unique polyreactive antibodies derived from HIV positive donors which bind multiple antigens (see abstract) wherein said antibodies have unique properties not found in conventional antibodies. The CDR3 grafted antibody also contains adjacent nonCDR3 amino acid residues found in the parental antibody which are deemed pertinent regarding the binding specificity of said antibody (see page 742, second column). It also contains framework regions that are found in other polyreactive antibodies with a similar specificity (see Figure 2). Regarding Polymenis et al., said reference also deals with autoantibodies which bind DNA. Furthermore, the antibody which received the CDR3 region only differed from the donor antibody by six amino acids (out of approximately 100 amino acids) outside of CDR3 (see Figure 2). Regarding Klimka et al., said reference discloses that the **CDR3 and framework4 regions are required** to maintain antigen specificity (see page 253, first column). Furthermore, Klimka et al. teach the hybrid antibody requires a use of a particular VH-1 amino acid sequence wherein the identity of said sequence is unpredictable prior to actually performing the experiment (see page 255, second column, last paragraph). Similar issues exist with regards to the Beiboer et al. reference. It is also noted the generated antibody contains numerous unpredictable mutations in the nonCDR3 regions in comparison to the germline human antibody sequence (see abstract). Regarding Rader et al., the disclosed antibodies require specific amino acids outside the CDR3 region (see Figure 2). In addition, the antibodies are generated using screening procedures wherein the identification of amino acids required for the antibody to function is unpredictable prior to the actual screening procedure.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 103,106-108,115,119,120,123,124,126,127, 129-134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Korman et al. (WO 01/14424) in view of Kucherlapti et al. (WO 96/33735).

Korman et al. teach IgG1 human antibodies made in transgenic mice that bind to a therapeutically relevant human cell surface antigen (see pages 8-9, 32-34) wherein said antibodies are made using the same transgenic mouse as per used by applicant in the specification (aka Hco7, see page 70-71). Antibodies produced via murine hybridomas are glycosylated. Korman et al. teach hybridomas producing said antibodies (see pages 32-34). Korman et al. teach a pharmaceutical composition containing one or more of said antibodies (see page 47) and additional therapeutic agents (see page 51). Korman et al. teach kits containing said antibodies (see page 65). Korman et al. do not teach that the antibody binds CD20. Kucherlapti et al. disclose that it is desirable to produce human antibodies made in transgenic mice that bind to human CD20 (see abstract). The antiCD20 antibodies made by the methods of Korman et al. would use the same transgenic mice (aka Hco7) as used in the specification, wherein said mice would produce antibodies with the same properties as those recited in the claims because the antibodies are made in the same transgenic mice (aka the mice use the

same transgenic human VH and VL, wherein said VH would contain the sequence recited in the claims and wherein said sequence is derived from an unmutated VH used by said transgenic mice). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Korman et al. teach IgG1 human antibodies made in transgenic mice that bind to a therapeutically relevant human cell surface antigen and methods of making such antibodies whilst Kucherlapti et al. disclose that it is desirable to produce human antibodies made in transgenic mice that bind to human CD20. One of ordinary skill in the art would have been motivate to do the aforementioned because Kucherlapti et al. disclose that it is desirable to produce human antibodies made in transgenic mice that bind to human CD20. Furthermore, in KSR Int'l Co. v. Teleflex Inc., 550 U.S. m, 2007 WL 1237837, at "13 (2007) it was stated that **"if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill"**.

Regarding applicants comments about unexpected results, the rejected claims encompass antibodies other than the 2F2 or 7D8 antibodies. The MPEP section 716.02(d) [R-2] states:

Unexpected Results Commensurate in Scope With Claimed Invention

Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support.".

In addition, the MPEP section 716.01(c)II states:

>II. < ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 15 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the

disclosed subject matter from the applicant.
Kucherlapti et al. disclose that it is desirable to produce human antibodies made in transgenic mice that bind to human CD20 (see abstract). The antiCD20 antibodies made by the methods of Korman et al. use the same transgenic mice (aka Hco7) as used in the specification, wherein said mice would produce antibodies with the same properties as those recited in the claims because the antibodies are made in the same transgenic mice (aka the mice use the same transgenic human VH and VL, wherein said VH would contain the sequence recited in the claims and wherein said sequence is derived from an unmutated VH used by said transgenic mice).

8. Claims 110,114 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is (571)272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Daniel Kolker can be reached on 571 272-0735. The fax phone number for

the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ron Schwadron/
Primary Examiner, Art Unit 1644

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